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Original Research Article

# Comparative Evaluation of Varying Doses of Dexmedetomidine for Attenuating Extubation Response in Patients Undergoing Open Cholecystectomy

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**Conflict of interest: Nil**

**Abstract:**

**Background:** Extubation can provoke significant hemodynamic and airway responses, particularly in abdominal surgeries like open cholecystectomy. Dexmedetomidine, an α2-adrenergic agonist, has been shown to attenuate these responses, but the optimal dose remains uncertain.

**Aim:** To compare the efficacy and safety of three different doses of dexmedetomidine (0.5 µg/kg, 0.75 µg/kg, and 1.0 µg/kg) in attenuating the extubation response in patients undergoing open cholecystectomy.

**Methods:** A prospective, randomized, double-blind study was conducted at the Department of Anaesthesiology, Phulo Jhano Medical College, Dumka, Jharkhand, India. A total of 84 ASA I/II patients undergoing open cholecystectomy were divided into three groups of 28. Dexmedetomidine was administered intravenously 15 minutes before extubation. Extubation quality, hemodynamic parameters, time to first rescue analgesia, and adverse events were recorded and reviewed.

**Results:** The doses of 0.75 µg/kg and 1.0 µg/kg improved extubation quality and hemodynamic instability compared to the dose of 0.5 µg/kg, although the highest dose of dexmedetomidine (1.0 µg/kg) was associated with greater bradycardia and hypotension. The dose of 0.75 µg/kg provides the best efficacy-safety profile.

**Conclusion:** Dexmedetomidine, at a dose of 0.75 µg/kg, provides the best combination of efficacy and safety in blunting extubation responses in patients having an open cholecystectomy.

**Keywords:** Analgesia, Cholecystectomy, Dexmedetomidine, Extubation response, Hemodynamic stability.

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## Introduction

Tracheal extubation is considered a dangerous and frequently overlooked phase of general anesthesia with particularly difficult physiological stress factors all of which are recognized to lead to significant airway reflexes [1]. Reflex sympathetic stimulation can be involved in extubation resulting in tachycardia, hypertension, coughing, and agitation that can lead to catastrophic effects in patients with cardiovascular or neurological compromise by rapidly increasing intracranial, intraocular, and intra-abdominal pressure. Overall, extubation is much more likely to be associated with respiratory and hemodynamic complications than intubation [2]. Thus, achieving smooth controlled extubation is an important part of safe anesthetic practice.

In patients undergoing open cholecystectomy, which often has longer surgical times and increased postoperative pain, the attenuation of the extubation response is even more pronounced [3]. The physiological stress response that takes place during emergence can lead to hemodynamic instability related to heart rate and blood pressure, which can increase the risk for myocardial ischemia, stroke, and other adverse events [4]. Although many pharmacological agents such as opioids, calcium antagonists, and beta-adrenergic antagonists have been tried to achieve this goal, the side effects of respiratory depression, delayed recovery, and insufficient clinical advance have led to studies with lesser-known agents.

Dexmedetomidine is a select α2 -adrenergic receptor agonist with numerous therapeutic applications, especially beneficial in minimizing the extubation response [5]. Aside from its central sympatholytic effects, dexmedetomidine decreases norepinephrine release, and has analgesic, anxiolytic, and sedative properties with minimal respiratory depression. There is currently evidence that suggests dexmedetomidine will dampen the hemodynamic spikes associated with extubation [6]. An area of clinical

inquiry is the optimal dexmedetomidine dosing for a proper balance of safety and effectiveness. A prospective, randomized, double-blinded, study by Awasthi et al. (2020) looked at three doses of dexmedetomidine (0.5 µg/kg, 0.75 µg/kg, and 1 µg/kg) in patients undergoing open cholecystectomy [7]. Their study noted the 0.75 µg/kg and 1.0 µg/kg dexmedetomidine doses dampened the extubation response; however, the higher dose was associated with greater incidence of bradycardia, indicating a therapeutic window.

In the context of the above findings, the current study aims to further evaluate the efficacy and safety of different doses of dexmedetomidine in mitigating the cardiovascular and airway reactions of extubation. By assessing heart rate, blood pressure, extubation quality, level of sedation, and postoperative analgesic requirements, this goal is to uncover the best dose that balances the clinical efficacy with the least side effects. The benefits of this study could allude to being able ˙to provide better perioperative anesthesia care for open cholecystectomy and in general for higher-risk surgical procedures.

## Methodology

**Study Design and Setting:** This was a prospective, double-blind, randomized comparative study conducted in the Department of Anaesthesiology at Phulo Jhano Medical College, Dumka, Jharkhand, India for one year

**Sample Size:** A total of 84 patients scheduled for elective open cholecystectomy under general anesthesia were enrolled in the study.

**Randomization and Group Allocation:** Patients were randomly allocated into three equal groups (n = 28 each) using a computer-generated random number table. The study drug solutions were prepared by an independent anesthesiologist not involved in patient management or data collection. Each patient received a 10 mL infusion of the assigned dose of dexmedetomidine diluted in normal saline over 10 minutes using an infusion pump before extubation.

- **Group A**: Dexmedetomidine 0.5 µg/kg
- **Group B**: Dexmedetomidine 0.75 µg/kg
- **Group C**: Dexmedetomidine 1.0 µg/kg

**Anesthetic Protocol:** All patients were premedicated with tablet alprazolam 0.5 mg and ranitidine 150 mg the night before surgery and at 6:00 AM on the day of surgery. In the operating room, standard monitoring including ECG, NIBP, $SpO_2$, and BIS was instituted. Anesthesia was induced with thiopentone sodium (5 mg/kg) and fentanyl (2 µg/kg), and intubation was facilitated with atracurium (0.5 mg/kg). Anesthesia was maintained with 0.5–1.5% isoflurane in 60% nitrous oxide and oxygen. Atracurium was given intermittently for muscle relaxation. Dexmedetomidine infusion was started at the beginning of rectus sheath closure. Isoflurane was discontinued at the end of the surgery, and nitrous oxide was stopped before extubation. Residual neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg).

### Outcome Measures

#### Primary Outcomes

- Change in heart rate (HR) during and after extubation.
- Systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP).
- Peripheral oxygen saturation ($SpO_2$).
- Quality of extubation, assessed using a standardized 5-point extubation scale.

#### Secondary Outcomes

- Sedation levels, assessed using the Ramsay Sedation Scale at regular intervals post-extubation.
- Postoperative pain scores using the Visual Analogue Scale (VAS).
- Time to first rescue analgesic requirement after extubation.
- Total number of rescue analgesics administered within the first two hours.
- Incidence of adverse effects including bradycardia, hypotension, desaturation, coughing, and laryngospasm.

**Statistical Analysis:** Statistical analysis was conducted using IBM SPSS Statistics software (version XX). Continuous variables were expressed as mean ± standard deviation (SD) and analyzed using one-way ANOVA or the Kruskal-Wallis test, based on the normality of data distribution. Categorical variables were presented as frequencies and percentages, and comparisons among groups were performed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant. Post hoc analysis with appropriate corrections was applied where necessary to identify intergroup differences.

## Results

This section presents the results of the study, highlighting the comparative effects of three different doses of dexmedetomidine on extubation response in patients undergoing open cholecystectomy. Main outcome measures were the comparability of demographics, extubation quality, peri-extubation hemodynamic parameters, postoperative analgesic requirements and incidence of complications.

Table 1 demonstrates the demographic characteristics of the study population in the three groups who received the three different doses of dexmedetomidine. In terms of mean age, there was no statistical significance (p= 0.72) between the groups (adequate

p value lower than 0.05 indicates groups' base line comparability) between group A; 42.6 ± 10.5 years, group B; 41.8 ± 11.1 years, and group C; 43.2 ± 9.8 years. For demographic gender distribution (M/F); 7/21, 6/22, and 8/20 respectively, there was an adequate p value (p = 0.81). Mean BMI values were also comparable in our study' population across each group; group A BMI; 25.4 ± 2.0 kg/m², group B BMI; 25.1 ± 2.2 kg/m², and group C BMI; 25.7 ± 1.9 kg/m² (p= 0.65). ASA physical status was also comparable based on 1-2 classification in each group (p= 0.87). Thus, it was a good demographic match.

**Table 1: Demographic Characteristics of the Study Population (Mean ± SD or Frequency)**

| Parameter | Group A (0.5 µg/kg) | Group B (0.75 µg/kg) | Group C (1 µg/kg) | p-value |
|---|---|---|---|---|
| Age (years) | 42.6 ± 10.5 | 41.8 ± 11.1 | 43.2 ± 9.8 | 0.72 |
| Gender (M/F) | 7/21 | 6/22 | 8/20 | 0.81 |
| BMI (kg/m²) | 25.4 ± 2.0 | 25.1 ± 2.2 | 25.7 ± 1.9 | 0.65 |
| ASA I/II | 13/15 | 14/14 | 12/16 | 0.87 |

Table 2 presents the quality of extubation across the three groups based on a 5-point scale. In Group A (0.5 µg/kg), only 7 patients experienced no coughing, while in Groups B (0.75 µg/kg) and C (1 µg/kg), 13 and 14 patients, respectively, had no coughing, indicating a better extubation profile at higher doses. Minimal coughing was observed in 9, 11, and 10 patients in Groups A, B, and C, respectively. Moderate coughing was more frequent in Group A (10 patients) compared to only 3 patients each in Groups B and C. Severe coughing occurred in 2 patients in Group A and in 1 patient each in Groups B and C. Notably, no cases of poor extubation were recorded in any group. These findings suggest that higher doses of dexmedetomidine (0.75 µg/kg and 1 µg/kg) were associated with smoother extubation and better suppression of airway reflexes compared to the lower dose.

**Table 2: Quality of Extubation**

| Extubation Quality Score | Group A (n = 28) | Group B (n = 28) | Group C (n = 28) |
|---|---|---|---|
| No coughing | 7 | 13 | 14 |
| Minimal coughing | 9 | 11 | 10 |
| Moderate coughing | 10 | 3 | 3 |
| Severe coughing | 2 | 1 | 1 |
| Poor extubation | 0 | 0 | 0 |

Table 3 illustrates the hemodynamic parameters at the time of extubation among the three study groups. Group A (0.5 µg/kg) exhibited significantly higher values for all measured parameters compared to Groups B (0.75 µg/kg) and C (1 µg/kg). The mean heart rate was highest in Group A (92.1 ± 8.4 bpm), followed by Group B (84.6 ± 7.9 bpm), and lowest in Group C (81.2 ± 8.1 bpm), with a statistically significant difference (p < 0.001). Similarly, systolic blood pressure (SBP) was markedly elevated in Group A (142.5 ± 12.3 mmHg) compared to Group B (128.4 ± 10.6 mmHg) and Group C (125.3 ± 11.0 mmHg). Diastolic blood pressure (DBP) and mean arterial pressure (MAP) followed the same trend, with Group A showing higher values (DBP: 88.2 ± 9.0 mmHg; MAP: 106.3 ± 8.5 mmHg) than Group B (DBP: 79.1 ± 7.8 mmHg; MAP: 95.5 ± 7.6 mmHg) and Group C (DBP: 77.4 ± 7.2 mmHg; MAP: 93.4 ± 7.1 mmHg). All differences were statistically significant (p < 0.001), indicating superior hemodynamic stability at higher dexmedetomidine doses during extubation.

**Table 3: Hemodynamic Parameters at Extubation (Mean ± SD)**

| Parameter | Group A | Group B | Group C | p-value |
|---|---|---|---|---|
| Heart Rate (bpm) | 92.1 ± 8.4 | 84.6 ± 7.9 | 81.2 ± 8.1 | <0.001 |
| SBP (mmHg) | 142.5 ± 12.3 | 128.4 ± 10.6 | 125.3 ± 11.0 | <0.001 |
| DBP (mmHg) | 88.2 ± 9.0 | 79.1 ± 7.8 | 77.4 ± 7.2 | <0.001 |
| MAP (mmHg) | 106.3 ± 8.5 | 95.5 ± 7.6 | 93.4 ± 7.1 | <0.001 |

Table 4 summarizes the postoperative analgesic requirements among the three groups. The time to first rescue analgesia was shortest in Group A (45.2 ± 13.8 minutes) and progressively longer in Group B (50.1 ± 12.6 minutes) and Group C (55.7 ± 14.2 minutes), with the difference reaching statistical significance (p = 0.04). This suggests that higher doses of dexmedetomidine provided a longer duration of postoperative analgesia. However, the total number of analgesics used within the observation period was comparable across all groups (2.4 ± 0.5 in Group A, 2.3 ± 0.5 in Group B, and 2.2 ± 0.4 in Group C), with no statistically significant difference (p = 0.31).

| Table 4: Time to First Rescue Analgesia and Number of Analgesics Used | | | | |
|---|---|---|---|---|
| **Parameter** | **Group A** | **Group B** | **Group C** | **p-value** |
| Time to first rescue analgesia (min) | 45.2 ± 13.8 | 50.1 ± 12.6 | 55.7 ± 14.2 | 0.04 |
| Total number of analgesics used | 2.4 ± 0.5 | 2.3 ± 0.5 | 2.2 ± 0.4 | 0.31 |

Table 5 presents the incidence of adverse events observed across the three study groups. Bradycardia was most frequent in Group C (1 µg/kg), affecting 9 patients, compared to 3 in Group B (0.75 µg/kg) and only 2 in Group A (0.5 µg/kg), indicating a dose-related increase in this side effect. Similarly, hypotension occurred more commonly in Group C (6 patients), followed by Group B (2 patients) and Group A (1 patient). Desaturation episodes ($SpO_2$ <95%) were infrequent but showed a mild increase with higher doses: 2 cases in Group C and 1 in Group B, with none in Group A. No incidents of laryngospasm were reported in any group. These findings suggest that while higher doses of dexmedetomidine are more effective in controlling extubation responses, they are also associated with a greater incidence of dose-dependent adverse effects, particularly bradycardia and hypotension.

| Table 5: Incidence of Adverse Events | | | |
|---|---|---|---|
| **Adverse Event** | **Group A (n = 28)** | **Group B (n = 28)** | **Group C (n = 28)** |
| Bradycardia | 2 | 3 | 9 |
| Hypotension | 1 | 2 | 6 |
| Desaturation (<95%) | 0 | 1 | 2 |
| Laryngospasm | 0 | 0 | 0 |

## Discussion

The current study assessed the efficacy and safety of three doses of dexmedetomidine (0.5 µg/kg, 0.75 µg/kg, and 1 µg/kg) for attenuation of extubation responses in respect to open cholecystectomy. There is no statistically significant difference in the demographic data within the groups, which means that all measurable differences in extubation response and hemodynamic parameters that emerged between groups were primarily secondary to the doses of dexmedetomidine they were allocated and not significant differences in baseline characteristics at the time of measurement.

The extubation quality improved with increasing doses of dexmedetomidine, and patients in the 0.75 µg/kg group and 1.0 µg/kg group experienced decreased incidence of coughing during extubation compared with patients in the 0.5 µg/kg dexmedetomidine group. This applies to the findings from Bindu et al with the study showing that the administration dexmedetomidine prior to extubation at a dose of 0.75 µg/kg provided diminution of airway reflexes response and a quality improvement of emergence for surgical patients [6]. Likewise, Selvaraj 2016 demonstrated improved condition during extubation and decreased incidence of coughing while comparing high dose dexmedetomidine to placebo [8].

All hemodynamic variables recorded during extubation (i.e., heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure) were significantly lower with the higher doses. Kim et al., 2016 showed that when utilizing dexmedetomidine at doses of ≥0.5 µg/kg, the sympathetic surge observed during extubation was significantly attenuated, without causing respiratory depression [9]. Similarly, Pradhan and Vaidya (2019) observed attenuation of airway and cardiovascular effects using dexmedetomidine at a dose of 0.5 µg/kg, in patients undergoing general surgical procedures [10]. Additionally, Keniya et al., 2011 observed significant reductions in heart rate and blood pressure during extubation in patients receiving a dose of 0.5 µg/kg dexmedetomidine, but reported a mild increase in incidence of hypotension [11].

Regarding postoperative analgesia, there was a significant delay in first rescue analgesic administration among patients receiving higher doses of dexmedetomidine; however, total analgesic consumption did not differ among patients. Kaye et al. 2020 reported similar findings in 2020 with respect to better postoperative comfort with reduced analgesic demand in the early postoperative period with dexmedetomidine administration [12]. However, the occurrence of adverse events was dose related, with significant bradycardia and hypotension occurring in the 1.0 µg/kg group. This is in line with the findings of Bindu et al., who noted that while higher doses improved extubation conditions, the cardiovascular side effects occurred more frequently and recovery time was greater [6].

Therefore, dexmedetomidine at a dose of 0.75 µg/kg appears to achieve the best balance between efficacy and safety in minimizing extubation responses. It allows better control of airway reflexes and hemodynamic parameters, prolonged analgesia, and an acceptable rate of adverse events. These findings support the ability for clinicians to use intermediate-dose dexmedetomidine in their anesthetic practices.

## Conclusion

The results of this study suggest that dexmedetomidine is good at blunting the extubation reflex after

open cholecystectomy surgery, with moderate dose-dependent changes in extubation quality, hemodynamic stability, and postoperative analgesia. Of the three doses used, 0.75 µg/kg represented the best efficacy to safety ratio by bluntly increasing extubation smoothness and improving hemodynamic control while maintaining a safety profile better than the 1.0 µg/kg group. The 0.5 µg/kg group was non-inferior in safety but was again less effective at blunting airway reflexes. These findings suggest that the use of intermediate dose dexmedetomidine may be considered the new standard for patients in emergence from general anesthesia who experience disjointed emergence common in performing open abdominal procedures.

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